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The effect of intrauterine transfusions for hemolytic disease of the fetus and newborn

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Objective

Hemolytic disease of the fetus and newborn (HDFN) can occur when maternal antibodies attack and destroy fetal erythrocytes leading to fetal anemia or even death. To correct the fetal anemia and prevent severe morbidity and mortality intrauterine transfusions (IUTs) are currently considered the cornerstone in treatment of severe HDFN. Different techniques can be used for IUT: vascular access via the umbilical vein at the placental cord insertion (UCP)or via the intrahepatic vein (IH). Lastly there is an option to give an (non-vascular) intraperitoneal deposition of donor blood. The last is also given in addition to a UCP or IH transfusion. In smaller cohort studies it has been suggested that leaving an intraperitoneal (IP) deposition of donor blood in addition to a vascular IUT has a beneficial effect and possibly prolongs the interval between transfusions. This additional deposition is most conveniently left after an IH transfusion if the syringe is withdrawn. In the current study we therefore aim to independently determine the effect of the IP transfusion blood deposition after an IH transfusion on the Hb values at the next IUT and the interval between IUTs.

Methods

A retrospective cohort study was conducted at the Leiden University Medical Hospital (LUMC) between November 2005 and December 2022. IUTs were classified as intrahepatic intravascular (IH), intrahepatic intravascular with IP (IH+IP), umbilical cord at placental insertion (UCP) or other. In a sub-cohort of patients uniformly treated at every subsequent IUT with one technique were divided in to three groups: UCP, IH and IH+IP. The decline in Hb (measured by comparing the Hb level directly after IUT with the Hb level determined before the subsequent IUT) and interval between transfusions were compared in the three groups. To independently compare the effect of IP on the Hb values and the interval between IUTs in the entire study population, both uniformly treated patients as non-uniformly treated patients, all transfusions in the cohort were compared using Generalized Estimated Equations (GEE).

Results

A total of 317 fetus received one or more transfusions leading to 812 transfusions in total. In the three uniformly treated groups, 96 fetus received 2 or more UCP transfusions, 14 fetus received 2 or more IH transfusions and 34 received 2 or more IH+IP transfusions. The mean decline in Hb in mg/dL/day was 0.16 in the UCP group (SD 0.138), 0.13 in the IH group (SD 0.104) and 0.10 in the IH+IP group (SD 0.097). The UCP group consistently had the shortest interval between IUTs. The interval of IH accumulates towards three weeks after five IUTs in comparison to UCP. IH+IP resulted in a more steady decline of Hb, but there was little difference with the IH group when comparing the interval between IUTs. Because the groups of patients who received five IUTs were small, a GEE will be performed including alle transfusions from the study population. The GEE is currently finalized and results will be added soon and available during the Congress in June.

Conclusion

This is the largest retrospective cohort study comparing different transfusion techniques for HDFN. We found that intravascular intrahepatic transfusions combined with an intraperitoneal deposit of transfusion blood result in a more steady Hb level compared to transfusions in the umbilical cord at placental insertion. The decline of Hb levels become increasingly steady when an IP deposition is added. In the uniformly treated sub-cohort, IP did not add on a clinical relevant prolongation of the interval between IUTs. However the results are still preliminary; correction for severity of disease and other baseline characteristics will be done by performing a GEE.